

Solid Tumour Section

Mini Review

Head and neck: Pleomorphic salivary gland adenoma with inv(8)(q12q12) (CHCHD7/PLAG1)

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Clinics and pathology

Disease

Pleomorphic salivary gland adenomas (PA) are benign, slow-growing tumors, which show a remarkable degree of morphological diversity. They constitute the most common form of all salivary gland neoplasms and the majority of the PAs occur in the parotid gland, while the remaining tumors are found in the submandibular and minor salivary glands. Although PAs are benign tumors, subsets of these tumors have a tendency to recur and/or undergo malignant transformation.

Cytogenetics

inv(8)(q12.1;q12.1)

Genes involved and Proteins

CHCHD7 (*Coiled-coil-helix-coiled-coil-helix domain containing 7*)

Location: 8q12.1

DNA/RNA

The gene spans about 7 kb and includes 5 exons. Six isoforms of RNA, spliced with or without exon 2, exist with transcript sizes ranging from 1575 bp to 1767 bp.

Protein

The protein contains a conserved CHCH domain and is included in a multifamily of proteins which show a strong conservation at the structural level but a low conservation at the amino acid level.

PLAG1 (*Pleomorphic Adenoma Gene 1*)

Location: 8q12

DNA/RNA

The gene spans 50 kb and includes 5 exons. The size of the transcript is about 7.3 kb. Two splicing forms of RNA have been found, with or without exon 2.

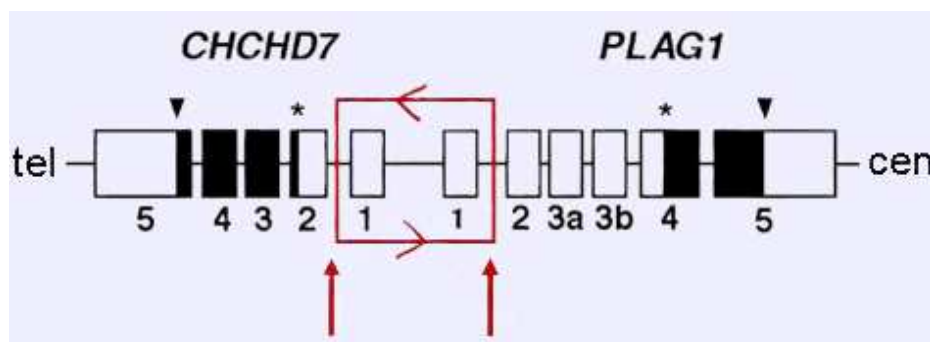
Protein

500 amino acids (aa), 74 kDa. The gene encodes a zinc finger protein with two putative nuclear localization signals. It contains a conserved SFP1 domain (aa 58-139), which is a putative transcriptional repressor regulating G2/M transition.

Result of the chromosomal anomaly

Hybride Gene

Note: The two genes CHCHD7 and PLAG1 are located head-to-head about 500 bp apart in 8q12. The fusion results from a cryptic, paracentric inversion.



Map of the 8q12 region including the CHCHD7 and PLAG1 genes (not drawn to scale). Exons are shown as boxes and the start and stop codons are shown as asterisks and arrowheads, respectively. Breakpoints are shown in red. Reprinted partially from publication CHCHD7-PLAG1 and TCEA1-PLAG1 gene fusions resulting from cryptic, intrachromosomal 8q rearrangements in pleomorphic salivary gland adenomas, *Genes Chromosomes Cancer*, Vol. 45, No. 9, 2006, 820-828. Copyright 2006 Wiley-Liss, Inc. Reprinted with permission of Wiley-Liss, Inc.

Description

The CHCHD7-PLAG1 fusion transcript is formed by fusion of exon 1 of CHCHD7 to exon 2 or 3 of PLAG1.

Detection protocols

RT-PCR using total RNA extracted from frozen tumor tissue. The CHCHD7-PLAG1 gene fusion was detected by amplification of cDNA using the primers CHCHD22S, 5'-GTGAGCCATTGACGTGTTTG-3' located in exon 1 of CHCHD7, and PLAG564AS, 5'-GGTTTCACCACGCTTACGTT3' located in exon 4 of PLAG1. Fusion transcripts of 467 and 362 bp were detected.

Fusion Protein

Description

Exon 1 of CHCHD7 fused to either exon 2 or 3 of PLAG1 results in a promoter swapping where the intact coding region of PLAG1 is expressed from a different promoter.

Expression Localisation

Nucleus.

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